# Clinical trial results:
# A Prospective, Randomized, Double-Blind Comparison of LY900014 to Humalog with an Open-Label Postprandial LY900014 Treatment Group in Children and Adolescents with Type 1 Diabetes
# PRONTO-PEDS

## Summary

| | |
|---|---|
| EudraCT number | 2018-002371-18 |
| Trial protocol | DK CZ DE FR GB AT ES PL IT |
| Global end of trial date | 02 July 2021 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 11 January 2022 |
| First version publication date | 11 January 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | I8B-MC-ITSB |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03740919 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16698 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559, |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 02 July 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 02 July 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The reason for this study is to compare the study drug LY900014 to insulin lispro (Humalog) in children and adolescents with type 1 diabetes (T1D).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 April 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 138 |
| Country: Number of subjects enrolled | Czechia: 60 |
| Country: Number of subjects enrolled | Japan: 12 |
| Country: Number of subjects enrolled | Ukraine: 138 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Spain: 52 |
| Country: Number of subjects enrolled | Russian Federation: 62 |
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | China: 23 |
| Country: Number of subjects enrolled | Brazil: 57 |
| Country: Number of subjects enrolled | Poland: 34 |
| Country: Number of subjects enrolled | Denmark: 1 |
| Country: Number of subjects enrolled | Italy: 39 |
| Country: Number of subjects enrolled | Mexico: 60 |
| Country: Number of subjects enrolled | Israel: 43 |
| Country: Number of subjects enrolled | France: 4 |
| Country: Number of subjects enrolled | Germany: 17 |
| Worldwide total number of subjects | 751 |
| EEA total number of subjects | 208 |

Notes:

| Subjects enrolled per age group | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 265 |
| Adolescents (12-17 years) | 486 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study included a 4-week lead-in period using open-label insulin-lispro (Humalog) followed by a 26-week double-blind treatment period (LY900014 and insulin lispro) and one open-label treatment arm (LY900014 Postmeal).

### Pre-assignment

Screening details:

The purpose of the lead-in period was to obtain blood glucose (BG) values along with basal and prandial insulin doses to assess basal and mealtime insulin dosing and to determine baseline hypoglycemia rates.

### Period 1

| | |
|---|---|
| Period 1 title | Lead-in Period |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Insulin Lispro (Humalog) Lead-in |

Arm description:

Participants were switched to open-label insulin lispro (Humalog) administered subcutaneously (SC), using a unit for unit conversion or the dose could have been determined based on investigator's clinical judgement.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Insulin Lispro |
| Investigational medicinal product code | LY275585 |
| Other name | Humalog |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Insulin lispro (Humalog) administered SC using unit for unit conversion or dose may be determined based on investigator's clinical judgement.

| **Number of subjects in period 1** | Insulin Lispro (Humalog) Lead-in |
|---|---|
| Started | 751 |
| Received at Least One Dose of Study Drug | 751 |
| Completed | 716 |
| Not completed | 35 |
| Physician decision | 2 |
| Consent withdrawn by subject | 10 |
| Study Task Too Burdensome | 1 |
| Withdrew Consent Due to Required Procedures | 1 |
| Due to Coronavirus Disease 2019 (COVID-19) | 18 |
| Lab Results Did Not Match Inclusion Criteria | 1 |

| | |
|---|---|
| Lost to follow-up | 1 |
| Protocol deviation | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | Treatment Period |
| Is this the baseline period? | Yes[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Insulin Lispro (Humalog) |

Arm description:

Participants received insulin lispro (Humalog) 100 units per milliliter (U/mL) administered SC 0 to 2 minutes before each meal with once or twice daily basal insulin. Preprandial insulin doses were individualized and titrated according to protocol-defined targets.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Insulin Lispro |
| Investigational medicinal product code | LY275585 |
| Other name | Humalog |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

100 U/mL administered SC  0 to 2 minutes before each meal.

| | |
|---|---|
| **Arm title** | LY900014 |

Arm description:

Participants received 100 U/mL LY900014 administered SC 0 to 2 minutes before start of the meal.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | LY900014 |
| Investigational medicinal product code | |
| Other name | Ultra-Rapid Lispro |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

100 U/mL LY900014 administered SC 0 to 2 minutes before start of the meal.

| | |
|---|---|
| **Arm title** | LY900014 Postmeal |

Arm description:

Participants received 100 U/mL LY900014 administered SC up to 20 minutes after the start of the meal.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | LY900014 |
| Investigational medicinal product code | |
| Other name | Ultra-Rapid Lispro |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

100 U/mL LY900014 administered SC up to 20 minutes after the start of the meal.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The 4-week Lead-in period allowed all enrolled participants to switch to Humalog to determine baseline hypoglycemia rates. Not all participants in the Lead-in period chose to continue into the treatment period and treatment period is considered the baseline period.

| **Number of subjects in period 2[2]** | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal |
|---|---|---|---|
| Started | 298 | 280 | 138 |
| Received at Least One Dose of Study Drug | 298 | 280 | 138 |
| Completed | 288 | 266 | 135 |
| Not completed | 10 | 14 | 3 |
| Terminated by Sponsor | 1 | - | - |
| Consent withdrawn by subject | 7 | 6 | 2 |
| Adverse event, non-fatal | - | 2 | - |
| Not Completing Diary | - | 1 | - |
| Insulin Painful to Participant | - | 1 | - |
| Due to COVID-19 Pandemic | - | 3 | 1 |
| Issue with Insulin Pump | 1 | - | - |
| Protocol deviation | 1 | - | - |
| Failure of Inclusion Criteria | - | 1 | - |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all participants in the Lead-in period chose to continue into the treatment period and treatment period is considered the baseline period.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Insulin Lispro (Humalog) |
| Reporting group description: | |
| Participants received insulin lispro (Humalog) 100 units per milliliter (U/mL) administered SC 0 to 2 minutes before each meal with once or twice daily basal insulin. Preprandial insulin doses were individualized and titrated according to protocol-defined targets. | |
| Reporting group title | LY900014 |
| Reporting group description: | |
| Participants received 100 U/mL LY900014 administered SC 0 to 2 minutes before start of the meal. | |
| Reporting group title | LY900014 Postmeal |
| Reporting group description: | |
| Participants received 100 U/mL LY900014 administered SC up to 20 minutes after the start of the meal. | |

| Reporting group values | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal |
|---|---|---|---|
| Number of subjects | 298 | 280 | 138 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 12.4 | 12.1 | 12.3 |
| standard deviation | ± 3.2 | ± 3.4 | ± 3.8 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 140 | 144 | 65 |
| Male | 158 | 136 | 73 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 6 | 6 | 0 |
| Asian | 20 | 13 | 7 |
| Native Hawaiian or Other Pacific Islander | 2 | 0 | 0 |
| Black or African American | 7 | 3 | 1 |
| White | 256 | 256 | 126 |
| More than one race | 4 | 0 | 1 |
| Unknown or Not Reported | 3 | 2 | 3 |
| Region of Enrollment<br>Units: Subjects | | | |
| United States | 51 | 55 | 25 |
| Czechia | 26 | 23 | 11 |
| Japan | 7 | 3 | 2 |
| Ukraine | 57 | 53 | 27 |
| United Kingdom | 3 | 5 | 2 |
| Spain | 21 | 19 | 8 |
| Russia | 23 | 21 | 12 |
| Austria | 1 | 0 | 0 |
| China | 11 | 7 | 4 |

| | | | |
|---|---|---|---|
| Brazil | 22 | 20 | 13 |
| Poland | 14 | 13 | 6 |
| Denmark | 0 | 1 | 0 |
| Italy | 15 | 15 | 6 |
| Mexico | 25 | 22 | 11 |
| Israel | 15 | 15 | 5 |
| France | 1 | 1 | 2 |
| Germany | 6 | 7 | 4 |
| HbA1c at Baseline | | | |
| Units: percent HbA1c | | | |
| arithmetic mean | 7.81 | 7.81 | 7.77 |
| standard deviation | ± 0.91 | ± 0.87 | ± 0.85 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 716 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 349 | | |
| Male | 367 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 12 | | |
| Asian | 40 | | |
| Native Hawaiian or Other Pacific Islander | 2 | | |
| Black or African American | 11 | | |
| White | 638 | | |
| More than one race | 5 | | |
| Unknown or Not Reported | 8 | | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| United States | 131 | | |
| Czechia | 60 | | |
| Japan | 12 | | |
| Ukraine | 137 | | |
| United Kingdom | 10 | | |
| Spain | 48 | | |
| Russia | 56 | | |
| Austria | 1 | | |
| China | 22 | | |
| Brazil | 55 | | |
| Poland | 33 | | |
| Denmark | 1 | | |
| Italy | 36 | | |
| Mexico | 58 | | |

| | | | |
|---|---|---|---|
| Israel | 35 | | |
| France | 4 | | |
| Germany | 17 | | |
| HbA1c at Baseline | | | |
| Units: percent HbA1c | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

## End points

### End points reporting groups

| Reporting group title | Insulin Lispro (Humalog) Lead-in |
|---|---|
| Reporting group description: | |
| Participants were switched to open-label insulin lispro (Humalog) administered subcutaneously (SC), using a unit for unit conversion or the dose could have been determined based on investigator's clinical judgement. | |
| Reporting group title | Insulin Lispro (Humalog) |
| Reporting group description: | |
| Participants received insulin lispro (Humalog) 100 units per milliliter (U/mL) administered SC 0 to 2 minutes before each meal with once or twice daily basal insulin. Preprandial insulin doses were individualized and titrated according to protocol-defined targets. | |
| Reporting group title | LY900014 |
| Reporting group description: | |
| Participants received 100 U/mL LY900014 administered SC 0 to 2 minutes before start of the meal. | |
| Reporting group title | LY900014 Postmeal |
| Reporting group description: | |
| Participants received 100 U/mL LY900014 administered SC up to 20 minutes after the start of the meal. | |

### Primary: Change from Baseline in Hemoglobin A1c (HbA1c) Efficacy Estimand at Week 26

| End point title | Change from Baseline in Hemoglobin A1c (HbA1c) Efficacy Estimand at Week 26[1] |
|---|---|

End point description:

Change from baseline in HbA1c was analyzed using mixed model repeated measures (MMRM) and includes fixed class effects of treatment, strata (pooled country, type of basal insulin, and age group), visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline value. An unstructured covariance structure will be used to model the within-participant errors.

The Efficacy Estimand included data collected prior to permanent discontinuation of study drug through Week 26.

Analysis Population Description (APD): All participants randomly assigned to study drug with baseline and at least one postbaseline measurement available while on study drug, per protocol.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline, Week 26

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, only participants who received Humalog and LY900014 administered before meals were included in the analysis.

| End point values | Insulin Lispro (Humalog) | LY900014 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 280 | 260 | | |
| Units: percentage of HbA1c | | | | |
| least squares mean (standard error) | 0.09 (± 0.052) | 0.06 (± 0.054) | | |

**Statistical analyses**

| **Statistical analysis title** | Change from Baseline in HbA1c Efficacy Estimand |
|---|---|
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 540 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[2] |
| P-value | = 0.783 |
| Method | Mixed models analysis |
| Parameter estimate | Least Squares Mean Difference (LS Mean) |
| Point estimate | -0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.17 |
| upper limit | 0.13 |

Notes:

[2] - Noninferiority margin [NIM]=0.4% for HbA1c

## Secondary: Change from Baseline in HbA1c (Postprandial) at Week 26

| End point title | Change from Baseline in HbA1c (Postprandial) at Week 26[3] |
|---|---|

End point description:

Change from baseline in HbA1c postprandial was analyzed using (MMRM and includes fixed class effects of treatment, strata (pooled country, type of basal insulin, and age group), visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline value. An unstructured covariance structure will be used to model the within-participant errors.

The Efficacy Estimand included data collected prior to permanent discontinuation of study drug through Week 26.

APD: All participants randomly assigned to study drug with baseline and at least one postbaseline measurement available while of study drug, per protocol.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 26

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, only participants who received Humalog administered before meals and LY900014 Postmeal were included in the analysis.

| **End point values** | Insulin Lispro (Humalog) | LY900014 Postmeal | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 280 | 131 | | |
| Units: percentage of HbA1c | | | | |
| least squares mean (standard error) | 0.09 (± 0.052) | 0.07 (± 0.076) | | |

**Statistical analyses**

| **Statistical analysis title** | Change from Baseline in HbA1c (Postprandial) |
|---|---|
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |

| | |
|---|---|
| Number of subjects included in analysis | 411 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[4] |
| P-value | = 0.867 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0.17 |

Notes:

[4] - NIM of 0.4%

## Secondary: Percentage of Participants With Documented Post-dose Hypoglycemic Events Within 1 and 2 Hours After the Prandial Dose

| | |
|---|---|
| End point title | Percentage of Participants With Documented Post-dose Hypoglycemic Events Within 1 and 2 Hours After the Prandial Dose |

End point description:

Documented post-dose hypoglycemia <54 milligrams per deciliter (mg/dL) and ≤ 70 mg/dL that occurred 1 and 2 hours after prandial dose.

APD: All randomized participants who received at least one dose of the randomly assigned study drug with non-missing baseline value and at least one non-missing post-baseline value of the response variable.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline through Week 26

| End point values | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: percentage of participants | | | | |
| least squares mean (standard error) | | | | |
| <54 mg/dL 1 Hour Post-dose | 26.50 (± 2.563) | 36.79 (± 2.891) | 29.70 (± 3.897) | |
| <54 mg/dL 2 Hour Post-dose | 54.04 (± 2.896) | 63.61 (± 2.883) | 57.88 (± 4.216) | |
| ≤70 mg/dL 1 Hour Post-dose | 49.67 (± 2.901) | 63.92 (± 2.874) | 48.51 (± 4.261) | |
| ≤70 mg/dL 2 Hour Post-dose | 77.03 (± 2.449) | 82.67 (± 2.267) | 70.29 (± 3.912) | |

### Statistical analyses

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 1-hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.13 |
| upper limit | 2.3 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 1-hour post-dose | |
| Comparison groups | LY900014 Postmeal v Insulin Lispro (Humalog) |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.487 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 1.83 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 1-hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.153 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.73 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 1.13 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 2-hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.02 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.06 |
| upper limit | 2.08 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 2-hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.455 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 1.76 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 2-hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |

| | |
|---|---|
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.259 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 1.19 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL 1-hour post-dose | |
| Comparison groups | LY900014 v Insulin Lispro (Humalog) |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.29 |
| upper limit | 2.51 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL 1-hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.822 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 1.43 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL 1-hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.35 |
| upper limit | 0.8 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL 2-hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.092 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 2.14 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL 2-hour post-dose | |
| Comparison groups | LY900014 Postmeal v Insulin Lispro (Humalog) |

| | |
|---|---|
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.133 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 1.11 |

| **Statistical analysis title** | Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL 2-hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.31 |
| upper limit | 0.8 |

## Secondary: Rate of Documented Post-dose Hypoglycemic Events Within 1 and 2 Hours After the Prandial Dose

| End point title | Rate of Documented Post-dose Hypoglycemic Events Within 1 and 2 Hours After the Prandial Dose |
|---|---|

End point description:

Documented post-dose hypoglycemia event is an event of blood glucose of < 54 mg/dL and ≤70 mg/dL that occurred within 1 and 2 hours after the prandial dose. The rate of documented hypoglycemia was estimated by a negative binomial regression including treatment and age group as independent variables and number of episodes as dependent variables with log (exposure/365.25 days) as the offset in the model.

APD: All randomized participants who received at least 1 dose of the randomly assigned study drug with non-missing baseline value and at least one non-missing post-baseline value of the response variable.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline through Week 26

| End point values | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: Events per participant per year | | | | |
| least squares mean (standard error) | | | | |
| < 54mg/dL 1 Hour Post-dose | 1.59 (± 0.251) | 2.04 (± 0.262) | 1.38 (± 0.287) | |
| < 54 mg/dL 2 Hour Post-dose | 4.48 (± 0.454) | 5.95 (± 0.510) | 6.17 (± 0.816) | |
| ≤70 mg/dL 1 Hour Post-dose | 6.54 (± 1.036) | 8.46 (± 0.992) | 5.29 (± 1.145) | |
| ≤70 mg/dL 2 Hour Post-dose | 19.0 (± 1.58) | 23.7 (± 1.86) | 21.1 (± 2.31) | |

**Statistical analyses**

| Statistical analysis title | Rate Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 1 hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.22 |
| Method | Negative binomial regression |

| Statistical analysis title | Rate Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 1-hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.599 |
| Method | Negative binomial regression |

| Statistical analysis title | Rate Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 1 hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |

| | |
|---|---|
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.112 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 2 hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.034 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 2 hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.055 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL 2 hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.814 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL 1 hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |

| | |
|---|---|
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.194 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL 1 hour post-dose | |
| Comparison groups | LY900014 Postmeal v Insulin Lispro (Humalog) |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.428 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 1 hr |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL 1 hour post-dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.057 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL 2 hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.056 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL 2 hour post-dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |

| | |
|---|---|
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.435 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate Documented Post-dose Hypoglycemic Events 2 hr |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL 2 hour post-dose | |
| Comparison groups | LY900014 Postmeal v LY900014 |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.404 |
| Method | Negative binomial regression |

## Secondary: Percentage of Participants With Documented Hypoglycemic Events

| End point title | Percentage of Participants With Documented Hypoglycemic Events |
|---|---|

End point description:

Documented hypoglycemia is defined as <54 mg/dL and ≤70 mg/dL respectively.

APD: All randomized participants who received at least one dose of the randomly assigned study drug with non-missing baseline value and at least one non-missing post-baseline value of the response variable.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline through Week 26

| **End point values** | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: percentage of participants | | | | |
| least squares mean (standard error) | | | | |
| <54 mg/dL | 80.81 (± 2.283) | 81.37 (± 2.329) | 74.45 (± 3.718) | |
| ≤70 mg/dL | 93.98 (± 1.375) | 92.55 (± 1.569) | 87.62 (± 2.806) | |

### Statistical analyses

| **Statistical analysis title** | Percentage Documented Hypoglycemic Events |
|---|---|
| Statistical analysis description:<br><54 mg/dL | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.864 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 1.57 |

| **Statistical analysis title** | Percentage Documented Hypoglycemic Events |
|---|---|
| Statistical analysis description:<br><54 mg/dL | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.132 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1.12 |

| **Statistical analysis title** | Percentage Documented Hypoglycemic Events |
|---|---|
| Statistical analysis description:<br><54 mg/dL | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.104 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.67 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.41 |
| upper limit | 1.09 |

| **Statistical analysis title** | Percentage Documented Hypoglycemic Events |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.489 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.42 |
| upper limit | 1.52 |

| **Statistical analysis title** | Percentage Documented Hypoglycemic Events |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.025 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.23 |
| upper limit | 0.9 |

| **Statistical analysis title** | Percentage Documented Hypoglycemic Events |
|---|---|
| Statistical analysis description:<br>≤70 mg/dL | |
| Comparison groups | LY900014 v LY900014 Postmeal |

| | |
|---|---|
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.099 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 1.11 |

## Secondary: Rate of Documented Hypoglycemia Events

| | |
|---|---|
| End point title | Rate of Documented Hypoglycemia Events |

End point description:

Documented hypoglycemia is defined as a hypoglycemic event of blood glucose of ≤70 mg/dL or <54 mg/dL. The rate of documented hypoglycemia was estimated negative binomial regression including treatment and age group as independent variables and number of episodes as dependent variable with log (exposure/365.25 days) as the offset in the model.

APD: All randomized participants who received at least 1 dose of the randomly assigned study drug with non-missing baseline value and at least one non-missing post-baseline value of the response variable.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Week 0 through Week 26

| End point values | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: events per participant per year | | | | |
| least squares mean (standard error) | | | | |
| < 54 mg/dL | 16.6 (± 1.23) | 16.1 (± 1.20) | 17.7 (± 1.99) | |
| ≤70 mg/dL | 78.0 (± 4.23) | 75.1 (± 4.44) | 76.1 (± 6.10) | |

## Statistical analyses

| Statistical analysis title | Rate of Documented Hypoglycemia Events |
|---|---|

Statistical analysis description:

< 54 mg/dL

| | |
|---|---|
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |

| | |
|---|---|
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.732 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate of Documented Hypoglycemia Events |
|---|---|
| Statistical analysis description:<br>< 54 mg/dL | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.638 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate of Documented Hypoglycemia Events |
|---|---|
| Statistical analysis description:<br><54 mg/dL | |
| Comparison groups | LY900014 Postmeal v LY900014 |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.462 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate of Documented Hypoglycemia Events |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.632 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate of Documented Hypoglycemia Events |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL | |
| Comparison groups | LY900014 Postmeal v Insulin Lispro (Humalog) |

| | |
|---|---|
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8 |
| Method | Negative binomial regression |

| **Statistical analysis title** | Rate of Documented Hypoglycemia Events |
|---|---|
| Statistical analysis description:<br>≤ 70 mg/dL | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.889 |
| Method | Negative binomial regression |

## Secondary: Rate of Severe Hypoglycemia

| End point title | Rate of Severe Hypoglycemia |
|---|---|

End point description:

Severe hypoglycemia: during these episodes, participants have an altered mental status and cannot assist in their own care, may be semiconscious or unconscious, or experience coma with or without seizures, and require assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions.

The rate of severe hypoglycemia per 100 years was calculated as: 100 times the total number of severe hypoglycemia episodes within the period divided by total exposure (in year) for all participants within the treatment group.

All randomized participants who received at least one dose of the randomly assigned study drug with non-missing baseline value and at least one non-missing post-baseline value of the response variable.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 0 through Week 26

| **End point values** | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: Per participant per 100 years | | | | |
| number (not applicable) | 2.05 | 2.20 | 0.00 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Insulin Dose at Week 26

| End point title | Change from Baseline in Insulin Dose at Week 26 |
|---|---|

End point description:

Change from baseline in insulin dose was analyzed using mixed model repeated measures (MMRM) and includes fixed class effects of treatment, strata (pooled country, type of basal insulin, age group, and HbA1c stratum (≤8.0%, >8.0%)), baseline value, visit and treatment-by-visit interaction. An unstructured covariance structure was used to model the within-participant errors.

APD: All participants randomly assigned to study drug with baseline and at least one postbaseline measurement available while on study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 26

| End point values | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 283 | 264 | 132 | |
| Units: Unit per day | | | | |
| least squares mean (standard error) | | | | |
| Total Daily Basal Insulin Dose | 2.3 (± 0.28) | 2.9 (± 0.29) | 2.7 (± 0.40) | |
| Total Daily Insulin Dose | 5.3 (± 0.66) | 5.8 (± 0.69) | 5.0 (± 0.96) | |

### Statistical analyses

| Statistical analysis title | Change from Baseline in Insulin Dose |
|---|---|

Statistical analysis description:

Total Daily Basal Insulin

| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
|---|---|
| Number of subjects included in analysis | 547 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 1.4 |

| Statistical analysis title | Change from Baseline in Insulin Dose |
|---|---|

| | |
|---|---|
| Statistical analysis description:<br>Total Daily Basal Insulin | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 415 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.404 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.5 |
| upper limit | 1.4 |

| **Statistical analysis title** | Change from Baseline in Insulin Dose |
|---|---|
| Statistical analysis description:<br>Total Daily Basal Insulin | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 396 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.693 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.2 |
| upper limit | 0.8 |

| **Statistical analysis title** | Change from Baseline in Insulin Dose |
|---|---|
| Statistical analysis description:<br>Total Daily Insulin Dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 547 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.625 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.5 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 2.3 |

| **Statistical analysis title** | Change from Baseline in Insulin Dose |
|---|---|
| Statistical analysis description:<br>Total Daily Insulin Dose | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 415 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.758 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6 |
| upper limit | 1.9 |

| **Statistical analysis title** | Change from Baseline in Insulin Dose |
|---|---|
| Statistical analysis description:<br>Total Daily Insulin Dose | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 396 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.485 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | 1.5 |

| **Secondary: Percentage of Participants with HbA1c < 7.0% and <7.5%** | |
|---|---|
| End point title | Percentage of Participants with HbA1c < 7.0% and <7.5% |
| End point description:<br>Percentage of participants with HbA1c < 7.0% and <7.5% was analyzed using a longitudinal logistic | |

regression with repeated measurements conducted by a generalized linear mixed model including independent variables of treatment, baseline HbA1c value, visit, baseline HbA1c-by-visit interaction, and treatment-by-visit interaction. An unstructured covariance structure was used.

APD: All participants who were randomly assigned to study drug and had non-missing baseline value and at least one non-missing post-baseline value of the response variable were included in the analysis.

| | |
|---|---|
| End point type | Secondary |
| End point timeframe: | |
| Week 26 | |

| **End point values** | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| HbA1c <7% | 20.00 | 21.92 | 19.08 | |
| HbA1c < 7.5% | 40.00 | 37.31 | 32.82 | |

**Statistical analyses**

| **Statistical analysis title** | Percentage HbA1c < 7.0% |
|---|---|
| Statistical analysis description: | |
| HbA1c < 7% | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.396 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 2 |

| **Statistical analysis title** | Percentage HbA1c < 7.0% |
|---|---|
| Statistical analysis description: | |
| HbA1c < 7% | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |

| | |
|---|---|
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.814 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.49 |
| upper limit | 1.75 |

| **Statistical analysis title** | Percentage HbA1c < 7.0% |
|---|---|
| Statistical analysis description:<br>HbA1c < 7% | |
| Comparison groups | LY900014 Postmeal v LY900014 |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.384 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.39 |
| upper limit | 1.43 |

| **Statistical analysis title** | Percentage HbA1c < 7.5% |
|---|---|
| Statistical analysis description:<br>HbA1c < 7.5% | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 |
| Number of subjects included in analysis | 578 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.55 |
| upper limit | 1.27 |

| **Statistical analysis title** | Percentage HbA1c < 7.5% |
|---|---|
| Statistical analysis description:<br>HbA1c < 7.5% | |
| Comparison groups | Insulin Lispro (Humalog) v LY900014 Postmeal |
| Number of subjects included in analysis | 436 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.094 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.36 |
| upper limit | 1.08 |

| **Statistical analysis title** | Percentage HbA1c < 7.5% |
|---|---|
| Statistical analysis description:<br>HbA1c < 7.5% | |
| Comparison groups | LY900014 v LY900014 Postmeal |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.306 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1.31 |

## Secondary: Change from Baseline in 7-Point Self-Monitored Blood Glucose (SMBG) Values at Week 26

| End point title | Change from Baseline in 7-Point Self-Monitored Blood Glucose (SMBG) Values at Week 26 |
|---|---|

End point description:

Change from baseline in 7-point SMBG values were analyzed using MMRM and includes fixed class effects of treatment, strata (pooled country, type of basal insulin, and age group, and HbA1c stratum (≤8.0%, >8.0%)) baseline value, visit, and treatment-by-visit interaction. An unstructured covariance structure was used to model the within-participant errors.

All participants randomly assigned to study drug with baseline and at least one postbaseline

measurement available while on study drug.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 26

| End point values | Insulin Lispro (Humalog) | LY900014 | LY900014 Postmeal | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 298 | 280 | 138 | |
| Units: milligram per dL (mg/dL) | | | | |
| least squares mean (standard error) | | | | |
| Morning Premeal-Fasting: n= 265, 247, 122 | 1.0 (± 2.78) | -3.4 (± 2.88) | -5.9 (± 4.11) | |
| Morning 1 hour Postmeal: n= 263, 239, 117 | -3.2 (± 2.92) | -17.9 (± 3.06) | -9.8 (± 4.39) | |
| Midday Premeal: n= 265, 247,122 | -3.1 (± 3.06) | 2.5 (± 3.17) | -6.0 (± 4.52) | |
| Midday 1 hour Postmeal: n= 262, 237, 120 | 0.9 (± 2.99) | -5.2 (± 3.14) | -1.5 (± 4.43) | |
| Evening Premeal: n= 264, 247,122 | 1.0 (± 3.18) | 4.6 (± 3.29) | 0.3 (± 4.69) | |
| Evening 1 hour Postmeal: n= 261, 234, 118 | 6.9 (± 3.22) | -6.2 (± 3.39) | -3.9 (± 4.79) | |
| Bedtime: n= 257, 240, 116 | -1.9 (± 3.03) | -2.3 (± 3.14) | -2.7 (± 4.53) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From Lead-in to Safety Follow-up (up to 32 Weeks) | |
| Adverse event reporting additional description: | |
| All randomized participants who receive at least 1 dose of study drug. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Humalog Lead-in |
| Reporting group description: | |
| Participants were switched to open-label Insulin lispro (Humalog) administered SC, using a unit for unit conversion or the dose may be determined based on investigator's clinical judgement. | |
| Reporting group title | LY900014 |
| Reporting group description: | |
| Participants received 100 Units per milliliter (U/mL) LY900014 administered SC 0 to 2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial insulin doses were individualized and titrated according to protocol-defined targets. | |
| Reporting group title | LY900014 Postmeal |
| Reporting group description: | |
| Participants received 100 U/mL LY900014 administered SC up to 20 minutes after the start of the meal. | |
| Reporting group title | Insulin Lispro (Humalog) |
| Reporting group description: | |
| Participants received 100 U/mL Insulin lispro (Humalog) administered subcutaneously (SC) 0 to 2 minutes before each meal with once or twice daily basal insulin. Preprandial insulin doses were individualized and titrated according to protocol-defined targets. | |

| Serious adverse events | Humalog Lead-in | LY900014 | LY900014 Postmeal |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 751 (0.27%) | 6 / 280 (2.14%) | 2 / 138 (1.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| reactive gastropathy | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| skin laceration | | | |
| alternative dictionary used: | | | |

| | | | |
|---|---|---|---|
| MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| macroglossia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 1 / 280 (0.36%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoglycaemic coma | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| anaphylactic reaction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| abdominal pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 1 / 280 (0.36%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastritis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| mental disorder | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 751 (0.13%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| complicated appendicitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 1 / 138 (0.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pilonidal cyst | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 751 (0.00%) | 1 / 280 (0.36%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| diabetic ketoacidosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 2 / 280 (0.71%) | 1 / 138 (0.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hyperglycaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 751 (0.00%) | 0 / 280 (0.00%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoglycaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 751 (0.13%) | 3 / 280 (1.07%) | 0 / 138 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Insulin Lispro (Humalog) | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 298 (4.03%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| reactive gastropathy | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| skin laceration | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spinal fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| macroglossia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 298 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hypoglycaemic coma | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| anaphylactic reaction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 298 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastritis | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychiatric disorders | | | | |
| mental disorder | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 0 / 298 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| complicated appendicitis | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 0 / 298 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastroenteritis | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pilonidal cyst | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| upper respiratory tract infection | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 298 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| diabetic ketoacidosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 298 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hyperglycaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hypoglycaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 298 (0.67%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | Humalog Lead-in | LY900014 | LY900014 Postmeal |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 39 / 751 (5.19%) | 67 / 280 (23.93%) | 21 / 138 (15.22%) |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 751 (0.80%) | 13 / 280 (4.64%) | 5 / 138 (3.62%) |
| occurrences (all) | 6 | 22 | 5 |
| General disorders and administration site conditions | | | |
| injection site reaction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 751 (0.13%) | 11 / 280 (3.93%) | 2 / 138 (1.45%) |
| occurrences (all) | 1 | 14 | 2 |
| Gastrointestinal disorders | | | |
| vomiting | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 751 (0.13%) | 9 / 280 (3.21%) | 3 / 138 (2.17%) |
| occurrences (all) | 1 | 10 | 3 |
| Infections and infestations | | | |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 21 / 751 (2.80%) | 28 / 280 (10.00%) | 7 / 138 (5.07%) |
| occurrences (all) | 21 | 37 | 9 |
| rhinitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 751 (0.93%) | 6 / 280 (2.14%) | 4 / 138 (2.90%) |
| occurrences (all) | 7 | 6 | 5 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 751 (0.40%) | 15 / 280 (5.36%) | 2 / 138 (1.45%) |
| occurrences (all) | 3 | 17 | 3 |

| **Non-serious adverse events** | Insulin Lispro (Humalog) | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 60 / 298 (20.13%) | | |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 13 / 298 (4.36%) | | |
| occurrences (all) | 21 | | |
| General disorders and administration site conditions | | | |
| injection site reaction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 298 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| vomiting | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 9 / 298 (3.02%) | | |
| occurrences (all) | 11 | | |
| Infections and infestations | | | |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 23 / 298 (7.72%) | | |
| occurrences (all) | 30 | | |
| rhinitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 10 / 298 (3.36%) | | |
| occurrences (all) | 10 | | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 16 / 298 (5.37%) | | |
| occurrences (all) | 18 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported